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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/876,375	06/06/2001	John G.K. Williams	20031000820	8990

20350 7590 10/09/2003

TOWNSEND AND TOWNSEND AND CREW, LLP  
TWO EMBARCADERO CENTER  
EIGHTH FLOOR  
SAN FRANCISCO, CA 94111-3834

EXAMINER

STRZELECKA, TERESA E

ART UNIT PAPER NUMBER

1637

DATE MAILED: 10/09/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Applicati n No.

09/876,375

Applicant(s)

WILLIAMS ET AL.

Examiner

Teresa E Strzelecka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-14,16-28 and 55-60 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 18-28 is/are allowed.
- 6) ☒ Claim(s) 1-14,16,17,55 and 57-60 is/are rejected.
- 7) ☒ Claim(s) 56 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on June 9, 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. This office action is in response to an amendment filed on June 9, 2003. Claims 1-14 and 16-28 were previously pending. Applicants added claims 55-60. Claims 1-14, 16-28 and 55-60 will be examined.
2. Applicants' arguments regarding rejection of claims 18-23 and 28 under 35 U.S.C. 102(e) over Prudent et al. were found persuasive, therefore this rejection is withdrawn. Applicants' arguments regarding the provisional double-patenting rejection were considered, but since other rejections are still pending, the provisional double-patenting rejection over claims of co-pending application No. 09/876,374 is maintained.
3. The drawings were received on June 9, 2003. These drawings are accepted.
4. This office action is made non-final because of new grounds for rejection.

### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:  

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
6. Claims 1-14, 16, 17, 58 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-14, 16, 17 are indefinite in claim 1. Claim 1 is indefinite because it is not clear what is the meaning of the limitation "intact NP probe". The claim's preamble states "A method for separating an intact NP probe from a phosphate detectable moiety...", whereas in step a) there is "...enzymatic cleavage of said intact NP probe...", and in step b) there is separation of phosphate detectable moiety from intact NP probe. An intact NP probe comprises the phosphate detectable

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moiety, therefore it is not clear how enzymatically cleaved NP probe can still be intact and undergo separation from the phosphate detectable moiety.

B) Claim 58 is indefinite because of a recitation of “said phosphate fluorophore moiety is a used for a member”. It is not clear what this phrase means.

C) Claim 60 is indefinite over the recitation of “phosphate detectable moieties are separated from said plurality of intact NP probes”. It is not clear how a phosphate detectable moiety, which is a part of an intact NP probe, can be separated from a still intact NP probe, i.e., how can a probe from which a phosphate detectable moiety has been removed remain intact.

***Claim interpretation***

7. Before proceeding with the rejection, Applicants’ definition of a charge-switch NP probe is provided:

“The term “charge-switch nucleotide” as used herein refers to a labeled nucleotide phosphate (e.g., .gamma.-NP-Dye) that upon release or cleavage of a phosphate detectable moiety (e.g., PPi-Dye) has a different net charge associated with the cleavage product compared to the intact nucleotide phosphate probe (e.g., .gamma.-NP-Dye).” (page 7, lines 28-31).

“The phrase “phosphate detectable moiety” refers to a detectable cleavage product from a NP probe of the present invention. Examples include, but are not limited to, PPi-Dye, PP-F, P-Dye, a phosphate fluorophore moiety, a terminal phosphate fluorophore moiety, a detectable moiety, charged groups, electrically active groups, detectable groups, reporter groups, combinations thereof, and the like.” (page 8, lines 6-10).

8. Applicants define energy fields as electric fields or pressure fields (page 5, lines 17 and 18).

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9. The phrase “polymerase is immobilized in single molecule configuration” is interpreted as multiple polymerase molecules, each of which is immobilized on a solid support.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 1, 5, 6, 10, 11, 13, 55, 57, 59 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Hyman (Anal. Bioch., vol. 174, pp. 423-436, 1988; cited in the IDS).

Regarding claim 1, Hyman teaches a method for sequencing DNA, the method comprising:

a) providing a sample comprising an intact NP probe with a detectable moiety attached thereto, whereupon an enzymatic cleavage of said intact NP probe to incorporate said NP probe on a primer strand hybridized to a target nucleic acid, a phosphate detectable moiety is produced, wherein said phosphate detectable moiety carries a molecular charge which is different than the molecular charge which is different than the molecular charge of said intact NP probe

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(Hyman teaches providing a solution comprising one of four dNTPs (= intact NP probes) and pumping such solution through a column containing immobilized template-primer-DNA polymerase complex. Upon incorporation of a correct dNTP into a primer strand Ppi (=a phosphate detectable moiety) is produced. Hyman does not specifically teach that the phosphate detectable moiety carries a molecular charge which is different from the molecular charge of the intact dNTP, but since a nucleotide triphosphate has a net charge of  $-3$ , after cleavage of two negative charges of Ppi, the Ppi has a charge of  $-2$ , which is different from the charge of intact dNTP ( page 423, second and third paragraphs, Fig. 1).); and

b) applying an energy field to said sample, thereby separating said phosphate detectable moiety from said intact NP probe (Hyman teaches applying a flow pressure field to the column to separate the Ppi from the template-primer-DNA polymerase complex, where the dNMP has been incorporated (page 425, 8<sup>th</sup> paragraph).

Regarding claim 5, Hyman teaches incorporation of dNTPs into a primer strand hybridized to a target nucleic acid using a DNA polymerase and release of Ppi (page 423, second paragraph).

Regarding claim 6, Hyman teaches immobilized DNA polymerase (page 423, third paragraph).

Regarding claim 10, Hyman does not specifically teach that the charge of Ppi is grater than the charge of the intact NP probe, but since the intact dNTP has a charge of  $-3$  and Ppi has a charge of  $-2$ , the charge of Ppi is greater than a charge of intact NP probe.

Regarding claim 11, Hyman does not specifically teach that the charge of Ppi is less than the charge of the intact NP probe, but since the intact dNTP has a charge of  $-3$  and Ppi has a charge of  $-2$ , in terms of absolute values the charge of Ppi is less than a charge of intact NP probe.

Regarding claim 13, Hyman teaches detection of Ppi (page 424, first paragraph; Fig. 1).

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Regarding claim 55, Hyman teaches a method of sequencing a nucleic acid (DNA), by providing a target nucleic acid, a polymerase priming moiety (= primer) a polymerase (=DNA polymerase) and a plurality of intact NP probes (= dNTPs) (page 423, first and second paragraphs),

mixing the target nucleic acid, primer, polymerase and dNTPs under conditions permitting target dependent polymerization of plurality of dNTPs under conditions capable of providing a time sequence of a plurality of phosphate detectable moieties (page 423, second paragraph; Fig. 1; page 426, 4th paragraph; Fig. 8); and

detecting over time plurality of phosphate detectable moieties to provide a sequence of target nucleic acid (Fig. 8).

Regarding claim 57, Hyman teaches PPis (pyrophosphates) (page 423, second paragraph).

Regarding claim 59, Hyman teaches DNA polymerase immobilized on DEAE-Sepharose beads (page 423, third paragraph; page 425, second paragraph).

Regarding claim 60, Hyman teaches separation of PPis from the incorporated dNMPs (page 424, first paragraph).

### ***Double Patenting***

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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13. Claims 1-14 and 16-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22-36 of copending Application No. 09/876,374.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 22 of the 09/876,374 is a species of claims 1 and 18 of the current application, therefore claims 1 and 18 are anticipated by claim 22 of the 09/876,374 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. No references were found teaching or suggesting claims 2-4, 7-9, 12, 14, 16-28, 56 and 58. Claims 18-28 are allowed. Claims 2-4, 7-9, 12, 14, 16, 17 and 58 are rejected for reasons given above.

15. Claim 56 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.



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***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

TS  
October 6, 2003

  
**JEFFREY FREDMAN**  
**PRIMARY EXAMINER**